UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,496	01/31/2002	Eldon Emberly	15157	5187

20844 7590 07/25/2005

NEC LABORATORIES AMERICA, INC.
4 INDEPENDENCE WAY
PRINCETON, NJ 08540

EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,496	EMBERLY ET AL.	
	Examiner	Art Unit	
	Cheyne D. Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 03, 2005 has been entered.
2. Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
3. Applicant's summary of the interview, February 23, 2005, has been accepted.
4. The cancellation of claims 26 and 27 has been acknowledged.
5. Claims 1-25 and 28 are examined on the merits.

CLAIM REJECTIONS - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-25 and 28 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory algorithm type subject matter.

8. Claims 1-25 and 28 are rejected because said claims are directed to a method comprising algorithmic steps for manipulating data such as protein backbone configuration without any physical alteration step, which is considered to be non-statutory subject matter. A reasonably interpretation of the instant invention, as supported by the instant specification, is that said invention is directed to a computational method (page 9, lines 3-6) for implementing the algorithms described on pages 11-16. Therefore, the instant invention has been reasonably construed as being directed to nonstatutory subject matter because the claimed invention is directed algorithmic steps for manipulating data without any physical alteration step. "For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory." (MPEP § 2106 (IV)(B)(2) (b), part ii). Similar to the nonstatutory example above, the instant invention comprises algorithmic steps for manipulating data such as protein backbone configuration without any physical alteration resulted from said algorithmic steps.

CLAIM REJECTIONS - 35 USC § 112 FIRST PARAGRAPH

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-25 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. NEW MATTER REJECTION.

11. Claim 1, lines 1-5, recites the limitation of "novel designable protein...which differ from known natural or man-made protein backbone configurations...elements" which has not been found in the instant specification. The pointed to support on page 9, lines 14-20, provides written basis for the limitations of "spatial arrangement and/or connectivity of secondary structural elements", lines 4-5. However, said support does not provide written basis for the claimed invention as a whole which is directed to "identifying novel...which differ from known natural or man-made protein backbone configurations..." Further, the instant specification discloses the goal of the instant invention "was to identify stacks with no natural counterparts as candidates for the design of novel protein folds..." (page 22, lines 17-21) which is different from the proposed amendment.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-25 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. The relative limitations "novel" and "known," in claim 1, lines 1 and 3, are vague and indefinite due to lacking any metes and bounds as to what suitability characteristic is

being evaluated in order to compare to less suitable attributes so as to evaluate what is "novel" or "known." Claims 2-25 and 28 are rejected for being dependent from claim 1.

15. Steps (a) through (c) of claim 1 are vague and indefinite because the antecedent basis for the "amino acid secondary structural elements" being utilized in said steps is not clear. For example, the preamble recites "novel designable protein backbone configurations" and "known natural or man-made protein backbone configurations", however, it is not clear whether steps (a) through (c) are directed to the "novel protein..." or "known natural...protein..." Claims 2-25 and 28 are rejected for being dependent from claim 1.
16. Claim 23, line 5, recites the limitation of "n=1-500" which causes said claim to be vague and indefinite because it is not clear whether "n" is between 1 to 500, or "n" is equal to 1 minus 500 (1-500).
17. Claim 28, line 4, recites the limitation of "the average number of sequences per stack" which causes said claim to be vague and indefinite because the antecedent basis for said limitation is not clear. For example, claim 1 from which claim 28 depends does not recite the calculation of "the average number of sequence per stack," however, the "average number..." is required by claim 28.

CLAIM REJECTIONS - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1-7, 15, 20, 23, and 24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dahiyat et al. (1997).

RESPONSE TO ARGUMENTS

20. Applicant argues Dahiyat et al. does anticipate the claimed invention as recited by the instant claims, especially claim 1. Further, Applicant points to page 82 and Figure 6 of Dahiyat et al. to argue that the method of Dahiyat et al. is directed to "identifying a new sequence of amino acids that will adopt a prespecified, previously known, and naturally occurring backbone configuration." Applicant's argument is not persuasive because the amendment in the preamble does not "give life, meaning, and vitality" to the claim; therefore, the new limitation is not given any patentable weight in regard to the prior art. For example, the argued limitation is recited in the preamble, however, the body of the claim does not directly include the structure of the "novel designable protein backbone configurations which differ from known natural or man-made protein backbone configurations..." Further, "if the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim" (MPEP 2111.02 [R-2]). However, this is not the case for the instant claim 1.

BASIS FOR REJECTION

21. Dahiyat et al. discloses a method for designing stable and well-folded (backbone configurations) proteins with novel sequences wherein said method comprises specifying a protein having less than 30 residues containing sheet, helix, and turns structures (page 82, Abstract etc. and column 3, lines 32-34). The method of Dahiyat et al. is directed toward the screening of possible sequences for compatibility with the desired protein fold (designable) (page 82, column 1, lines 12-16) and select an amino acid sequence that will stabilize a target structure (designable) (page 82, column 2, lines 4-7), as in instant claim 1, step a, and claims 2-4.

22. The arrangement of these secondary structural elements is directed to the core and boundary position of the protein in regard to side chains, protein coil-coil designs, and hairpin turns (stack as defined by the instant specification) (page 83, column 1 to column 2, line 19; and Figure 4), as in instant claim 1, steps b and c.

23. An alignment of the sequences indicates only 6 of the 28 residues are identical and four of the identities are in the buried cluster (page 83, column 3, lines 7-14), as in instant claims 5-7.

24. The method of Dahiyat et al. assesses backbone configurations the relative to a solvent-accessible surface residues (page 82, column 3, last paragraph). The NMR data were collected NMR spectrometry wherein water suppression was accomplished either with

pre-saturation during relaxation delay or pulsed filed gradients (page 87, References and Notes, No. 28), as in instant claim 15.

25. The total number of amino acid sequences that must be considered is the product of the number of possible amino acid at each residue position (page 83, column 1, lines 23-28) and the respective residues are classified by ranking (cluster) (Figure 1), as in instant claim 20.

26. The design algorithm of Dahiyat et al. designs proteins based on the following criteria distance restraint (constraint), protein-folding characteristics of a motif with a small hydrophobic ore, and the protein backbone is defined with a root-mean-square (rms) (page 85, columns 1-3, Experimental Validation §). Based on the criteria above, the design algorithm of Dahiyat et al. select for optimal sequence from nonoptimal sequences (Figure 1). The algorithm considers both hydrophobic and hydrophilic amino acids at boundary positions, whereas core positions and surface positions are restricted to hydrophilic amino acids (page 82, column 3, lines 16-21) which represent the limitation of "reduced to the hydrophobicities", as in instant claims 23 and 24.

CLAIM REJECTIONS - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

29. Claims 1-7, 9-11, 15, 16, 20, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahiyat et al. (1997) taken with Dahiyat et al. (US006403312B1).

RESPONSE TO ARGUMENTS

30. Applicant's argument directed to the primary reference, Dahiyat et al. (1997), has been fully considered and found to be unpersuasive as discussed in the above 35 USC §102(b) rejection. Further, on pages 14-15, Applicant argues Dahiyat et al. (US006403312B1) fails to disclose items a) and b). Applicant's argument is not persuasive because the argued limitations identified by items a) and b) are not in the claims. As for the limitations recited by the instant claims, Dahiyat et al. (1997) describes the limitations of claims 1-7, 15, 20, 23, and 24 as discussed above. Dahiyat et al. (US006403312B1) describes the limitations of claims 9-11 and 16 as discussed below. Therefore, claims 1-

7, 9-11, 15, 16, 20, 23, and 24 are obvious in view of Dahiyat et al. (1997) taken with Dahiyat et al. (US006403312B1).

BASIS FOR REJECTION

31. Dahiyat et al. (1997) describes the limitations of claims 1-7, 15, 20, 23, and 24 as discussed above.

32. However, Dahiyat et al. (1997) does not describe the step of generating an initial stack by the conjugate gradient method as in claims 9-11 and 16.

33. Dahiyat et al. (US006403312B1) describes a method for protein design comprising a step of using the conjugate gradient method for the computational prescreening process (column 30, Example 1). Dahiyat et al. (1997) describes the comparison of the FSD-1 and the design target is analyzed in stereoview using the best-fit superposition (symmetry) of the restrained energy minimized average NMR structure (Figure 6), as in instant claim 9-11 and 16.

34. Dahiyat et al. (1997) describes an improvement for designing stable, well-folded proteins with a fully automated novel sequence selection (Abstract etc. and page 82, column 1, lines 1-3).

35. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Dahiyat et al. (1997) to design stable, well-

folded proteins with a fully automated novel sequence selection using a protein library as taught by Dahiyat et al. (US006403312B1). Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to design stable, well-folded proteins with a fully automated novel sequence selection using a protein library as taught by Dahiyat et al. (1997) and Dahiyat et al. (US006403312B1).

CONCLUSION

36. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. The USPTO's official fax number is (571) 273-8300.

37. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables

applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

38. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

39. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

40. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

C. Dune Ly /CDL
7/19/05

Ardin H. Marschel 7/20/05
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER